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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN THE APPLICATION OF:

STEVEN GUTTERIDGE ET. AL.

CASE NO.: BB1533USNA

APPLICATION NO.: 10/668767

CONFIRMATION NO.: UNKNOWN

GROUP ART UNIT: UNKNOWN

EXAMINER: UNKNOWN

FILED: SEPTEMBER 23, 2003

FOR: ISOLATION AND USE OF RYANODINE RECEPTORS

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Alexandria, VA 22313-1450

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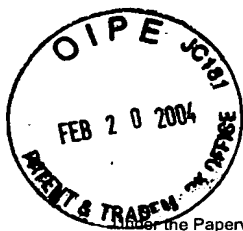
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Respectfully submitted,

JONATHON O. NARITA
AGENT FOR APPLICANTS
Registration No.: 53,369
Telephone: (302) 695-3127
Facsimile: (302) 695-3125

Dated: February 10, 2004

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10/668767

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| Filing Date | September 23, 2003 |
| First Named Inventor | Steven Gutteridge Et. Al. |
| Art Unit | UNKNOWN |
| Examiner Name | UNKNOWN |
| Attorney Docket Number | BB1533USNA |

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| | 1 | CHRISTOPHER H. GEORGE ET AL., Ryanodine Receptor Mutations Associated With Stress-Induced Ventricular Tachycardia Mediate Increased Calcium Release in Stimulated Cardiomyocytes, Circ. Res. 93:531-540, 2003 | <input type="checkbox"/> |
| | 2 | KINYA OTSU ET AL., Chromosome Mapping of Five Human Cardiac and Skeletal Muscle Sarcoplasmic Reticulum Protein Genes, Genomics, 17:507-509, 1993 | <input type="checkbox"/> |
| | 3 | GIUSEPPE GIANNINI ET AL., The Ryanodine Receptor/Calcium Channel Genes are Widely and Differentially Expressed in Murine Brain and Peripheral Tissues, The Journal of Cell Biology, 128(5):893-904, 1995 | <input type="checkbox"/> |
| | 4 | DAWEI JIANG ET AL., Enhanced Basal Activity of a Cardiac Ca ²⁺ Release channel (Ryanodine Receptor) Mutant Associated with Ventricular Tachycardia and Sudden Death, Circulation Research, 91:218-225, 2002 | <input type="checkbox"/> |
| | 5 | XUEHONG XU ET AL., Molecular Cloning of cDNA Encoding a Drosophila Ryanodine Receptor and Functional Studies of the Carboxyl-Terminal Calcium Release Channel, Biophysical Journal, 78:1270-1281, 2000 | <input type="checkbox"/> |
| | 6 | HIROSHI TAKESHIMA ET AL., Ca ²⁺ -induced Ca ²⁺ release in myocytes from dyspedic mice lacking the type-1 ryanodine receptor, The EMBO Journal 14(13):2999-3006, 1995 | <input type="checkbox"/> |

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| | | | | Art Unit | UNKNOWN |
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| | 7 | STEVEN O. MARX ET AL., PKA Phosphorylation Dissociates FKBP12.6 from the Calcium Release Channel (Ryanodine Receptor): Defective Regulation in Failing Hearts, Cell, Vol. 101:365-376, 2000 | <input type="checkbox"/> |
| | 8 | ANDREW J. DINSMORE ET AL., Characterisation of Antibody Models of the Ryanodine Receptor for Use in High-Throughput Screening, Pestic Sci., Vol. 54:345-352, 1998 | <input type="checkbox"/> |
| | 9 | TOSHIAKI IMAGAWA ET AL., Expression of Ca ²⁺ -Induced Ca ²⁺ Release Channel Activity from Cardiac Ryanodine Receptor cDNA in Chinese Hamster Ovary Cells, J. Biochem., Vol. 112:508-513, 1992 | <input type="checkbox"/> |
| | 10 | BARBARA BRUCE ET AL., Screening for Ryanodine Receptor Type 2 Mutations in Families with Effort-Induced Polymorphic Ventricular Arrhythmias and Sudden Death, J. of Amer. Coll. of Card., Vol. 40(2):341-349, 2002 | <input type="checkbox"/> |
| | 11 | GIAN ANTONIO DANELLI ET AL., Genetics of arrhythmogenic right ventricular cardiomyopathy, Current Opinion in Cardiology, Vol. 17:218-221, 2002 | <input type="checkbox"/> |
| | 12 | MIEKO SHIWA ET AL., Molecular Cloning and characterization of ryanodine receptor from unfertilized sea urchin eggs, Am. J. Physiol. Reg. Integrative Comp., Vol. 282:R727-R737, 2002 | <input type="checkbox"/> |

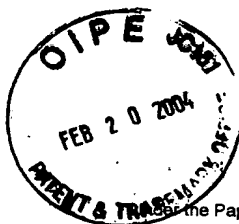
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| | 13 | YASUO OGAWA ET AL., Ryanodine Receptor Isoforms in Excitation-Contraction Coupling, Adv. Biophys., Vol. 36:27-64, 1999 | <input type="checkbox"/> |
| | 14 | G. LEES ET AL., Cell Culture Approaches to Invertebrate Neuroscience, Academic Press, New York, pp. 123-127, 1988 | <input type="checkbox"/> |
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| | 16 | MANJUNATHA B. BHAT ET AL., Functional Calcium release Channel Formed by the Carboxyl-Terminal Portion of Ryanodine Receptor, Biophysical J., Volume 73:1329-1336, 1997 | <input type="checkbox"/> |
| | 17 | NATASCIA TISO ET AL., The binding of the RyR2 calcium channel to its gating protein FKBP12.6 is oppositely affected by ARVD2 and VTSIP mutations, Biochem. & Biophys. Res. Comm., Vol. 299:594-598, 2002 | <input type="checkbox"/> |
| | 18 | ISAAC N. PESSAH ET AL., Calcium-Ryanodine Receptor Complex, The J. of Biol. Chem., Vol. 261(19):8643-8648, 1986 | <input type="checkbox"/> |

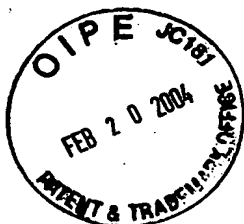
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| | 19 | ELISABETH LEHMBERG ET AL., Similarity of Insect and Mammalian Ryanodine Binding Sites, Pesticide Biochem. & Phys., 48:145-152, 1994 | <input type="checkbox"/> |
| | 20 | HIROSHI TAKESHIMA ET AL., Isolation and characterization of a gene for a ryanodine receptor/calcium release channel in Drosophila melanogaster, FEBS Letters, 337:81-87, 1994 | <input type="checkbox"/> |
| | 21 | NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION GENERAL IDENTIFIER NO. 456161, ACCESSION NO: D17389, MARCH 25, 1999, H. TAKESHIMA ET AL., Isolation and characterization of a gene for a ryanodine receptor/calcium release channel in Drosophila melanogaster | <input type="checkbox"/> |
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| | 24 | ELENA PUENTE ET AL., Identification of a polymorphic ryanodine receptor gene from Heliothis virescens (Lepidoptera: Noctuidae), Insect Biochem. & Mol. Biol., Vol. 30:335-347, 2000 | <input type="checkbox"/> |

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| | 26 | MARK D. ADAMS ET AL., The Genome Sequence of Drosophila Melanogaster, Science, Vol. 287:2185-2195,, 2000 | <input type="checkbox"/> |
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| | 29 | NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION GENERAL IDENTIFIER NO. 18656155, ACCESSION NO: BAB84714, FEBRUARY 14, 2002, M. SHIWA ET AL., Molecular cloning and characterization of ryanodine receptor from unfertilized sea urchin eggs | <input type="checkbox"/> |
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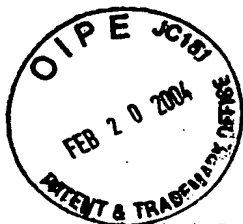
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| | 32 | PATRICK MOST ET AL., Transgenic Overexpression of the Ca2+-binding Protein S100A1 in the Heart Leads to Increased in Vivo Myocardial Contractile Performance, J. of Biol. Chem., Vol. 278(36):33809-33817, 2003 | <input type="checkbox"/> |
| | 33 | HUANG-TIAN YANG ET AL., The ryanodine receptor modulates the spontaneous beating rate of cardiomyocytes during development, PNAS, Vol. 99(14):9225-9230, 2002 | <input type="checkbox"/> |
| | 34 | ANNE-VALERIE FAURE ET AL., Developmental expression of the calcium release channels during early neurogenesis of the mouse cerebral cortex, European J. of Neuroscience, Vol. 14:1613-1622, 2001 | <input type="checkbox"/> |
| | 35 | MINGCAI ZHAO ET AL., Molecular Identification of the Ryanodine Receptor Pore-forming Segment, J. of Biol. Chem., Vol. 274(37):25971-25974, 1999 | <input type="checkbox"/> |
| | 36 | HIROSHI TAKESHIMA ET AL., Embryonic lethality and abnormal cardiac myocytes in mice lacking ryanodine receptor type 2, The EMBO J., Vol. 17(12):3309-3316, 1998 | <input type="checkbox"/> |

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|------------------------|---------------------------|
| Application Number | 10/668767 |
| Filing Date | September 23, 2003 |
| First Named Inventor | Steven Gutteridge Et. Al. |
| Art Unit | UNKNOWN |
| Examiner Name | UNKNOWN |
| Attorney Docket Number | BB1533USNA |

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|--------------------|-----------------------|---|--------------------------|
| | 37 | NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION GENERAL IDENTIFIER NO. 1245376, ACCESSION NO: AAA93465, APRIL 2, 1996, J. NAKAI ET AL., Primary structure and functional expression from cDNA of the cardiac ryanodine receptor/calcium release channel | <input type="checkbox"/> |
| | 38 | JUNICHI NAKAI ET AL., Primary structure and functional expression from cDNA of the cardiac ryanodine receptor/calcium release channel, FEBS Vol. 271(1,2):169-177, 1990 | <input type="checkbox"/> |
| | 39 | NATIONAL CENTER FOR BIOTECHNOLOGY INFORMATION GENERAL IDENTIFIER NO. 4506757, ACCESSION NO: NP001026, DECEMBER 23, 2003, C.H. GEORGE ET AL., Ryanodine receptor mutations associated with stress-induced ventricular tachycardia mediate increased calcium release in stimulated cardiomyocytes | <input type="checkbox"/> |
| | 40 | CHRISTOPHER H. GEORGE ET AL., Ryanodine receptor mutations associated with stress-induced ventricular tachycardia mediate increased calcium release in stimulated cardiomyocytes, J. of Biol. Chem., Vol. 278(31):28856-28864, 2003 | <input type="checkbox"/> |
| | 41 | JING ZHANG ET AL., Three-dimensional Localization of Divergent Region 3 of the Ryanodine Receptor to the Clamp-shaped Structures Adjacent to the FKBP Binding Sites, J. Biol. Chem., Vol. 278(16):14211-14218, 2003 | <input type="checkbox"/> |
| | 42 | HARUKO MASUMIYA ET AL., Localization of the 12.6-kDa FK506-binding Protein (FKBP12.6) Binding Site to the NH2-terminal Domain of the Cardiac Ca ²⁺ Release Channel (Ryanodine Receptor), J. Biol. Chem., Vol. 278(6):3786-3792, 2003 | <input type="checkbox"/> |

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|--------------------|-----------------------|---|--------------------------|
| | 43 | JIEFEI TONG ET AL., Caffeine and Halothane Sensitivity of Intracellular Ca ²⁺ Release is Altered by 15 Calcium Release Channel (Ryanodine Receptor) Mutations Associated with Malignant Hyperthermia and/or Central Core Disease, J. Biol. Chem., Vol. 272(42):26332-26339, 1997 | <input type="checkbox"/> |
| | 44 | S. R. WAYNE CHEN ET AL., Antibodies as Probes for Ca ²⁺ Activation Sites in the Ca ²⁺ Release Channel (Ryanodine Receptor) of Rabbit Skeletal Muscle Sarcoplasmic Reticulum, J. Biol. Chem., Vol. 268(18):13414-1421, 1993 | <input type="checkbox"/> |
| | 45 | CELETTA CALLAWAY ET AL., Localization of the High and Low Affinity [3H]Ryanodine binding Sites on the Skeletal Muscle Ca ²⁺ Release Channel, J. Biol. Chem., Vol. 269(22):15876-15884, 1994 | <input type="checkbox"/> |
| | 46 | MELANIE SCHMITT ET AL., Binding Sites for Ca ²⁺ -Channel Effectors and Ryanodine in Periplaneta americana - Possible Targets for New Insecticides, Pestic Science, Vol. 48:375-385, 1996 | <input type="checkbox"/> |
| | 47 | RICHARD E.A. TUNWELL ET AL., The human cardiac muscle ryanodine receptor-calcium release channel: identification, primary structure and topological analysis, Biochem. J. Vol. 318:477-487, 1996 | <input type="checkbox"/> |
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